What is Claimed:

1. A method of treating a patient undergoing a non-tissue graft therapy wherein the therapy may or does induce a deleterious immune response in the patient which method comprises administering to the patient a Cathepsin S inhibitor.

2. A method of treating a patient undergoing a non-tissue graft therapy wherein the therapy induces a deleterious immune response in the patient comprising administering to the patient a Cathepsin S inhibitor.

3. The method of Claim 1 or 2 wherein the therapy involves treatment of the patient with a small molecule therapeutic.

4. The method of Claim 3 wherein the small molecule therapeutic is heparin, low molecular weight heparin, procainamide, or hydralazine.

5. The method of Claim 1 or 2 wherein the therapy involes treatment of the patient with a biologic.

6. The method of Claim 5 wherein the biologic is a protein.

7. The method of Claim 5 wherein the biologic is an antibody.

8. The method of Claim 5 wherein the biologic is Remicade®, Refacto®, Referon-A®, Factor VIII, Factor VII, Betaseron®, Epogen®, Embrel®, Interferon beta, Botox®, Fabrazyme®, Elspar®, Cerezyme®, Myobloc®, Aldurazyme®, Verluma®, Interferon alpha, Humira®, Aranesp®, Zevalin® or OKT3.

9. A method of treating immune response in a patient caused by administration of a small molecule therapeutic or a biologic to the patient which method comprises administering to the patient in need of such treatment a therapeutically effective amount of a Cathepsin S inhibitor.

10. A method of treating a patient undergoing treatment with a biologic with a Cathepsin S inhibitor.

11. The method of Claim 9 wherein the immune response is caused by a small molecule therapeutic.

12. The method of Claim 11 wherein the small molecule therapeutic is heparin, low molecular weight heparin, procainamide, or hydralazine.

13. The method of Claim 9 wherein the immune response is caused by a biologic.

14. The method of Claim 10 or 13 wherein the biologic is a protein.

15. The method of Claim 14 wherein the biologic is an antibody.

16. The method of Claim 14 wherein the biologic is Remicade®, Refacto®, Referon-A®, Factor VIII, Factor VII, Betaseron®, Epogen®, Embrel®, Interferon beta, Botox®, Fabrazyme®, Elspar®,

Cerezyme®, Myobloc®, Aldurazyme®, Verluma®, Interferon alpha, Humira®, Aranesp®, Zevalin® or OKT3.

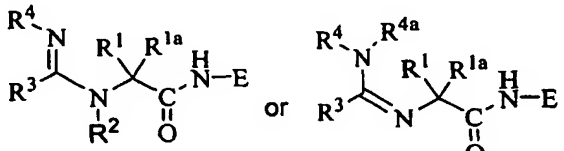
17. The method of any of the Claims 1-8 wherein the Cathepsin S inhibitor is administered prior to, concomitantly or after the therapy.

18. The method of any of the Claims 9, 11, or 12 wherein the Cathepsin S inhibitor is administered prior to, concomitantly, or after the administration of the small molecule therapeutic.

19. The method of any of the Claims 9, 10, and 13-16 wherein the Cathepsin S inhibitor is administered prior to, concomitantly, or after the administration of the biologic.

20. The method of any of the Claims 1-19 wherein the Cathepsin S inhibitor is:

(a) a compound of Formula (Ia) or (Ib):



(Ia) or (Ib)

wherein:

E is:

(i) $-C(R^5)(R^6)X^1$ where X^1 is -CHO, $-C(R^7)(R^8)CF_3$, $-C(R^7)(R^8)CF_2CF_2R^9$, $-C(R^7)(R^8)R^{10}$, $-C(O)C(O)R^{10}$, $-CH{=}CHS(O)_2R^{10}$, $-C(R^7)(R^8)C(R^7)(R^8)OR^{10}$, $-C(R^7)(R^8)CH_2OR^{10}$, $-C(R^7)(R^8)C(R^7)(R^8)R^{10}$, $-C(R^7)(R^8)CH_2N(R^{11})SO_2R^{10}$, $-C(R^7)(R^8)CF_2C(O)NR^{10}R^{11}$, $-C(R^7)(R^8)C(O)NR^{10}R^{11}$, $-C(R^7)(R^8)C(O)N(R^{11})(CH_2)_2OR^{11}$, or $-C(R^7)(R^8)C(O)N(R^{11})(CH_2)_2NR^{10}R^{11}$, or

(ii) $-C(R^{5a})(R^{6a})CN$;

where:

R^5 and R^{5a} are independently hydrogen or alkyl;

R^6 and R^{6a} are independently selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl, -alkylene-X-R^{12} (where X is –O-, $-NR^{13}$-, $-S(O)_{n1}$-, $-CONR^{13}$-, $-NR^{13}CO$-, $-NR^{13}C(O)O$-, $-NR^{13}CONR^{13}$-, $-OCONR^{13}$-, $-NR^{13}SO_2$-, $-SO_2NR^{13}$-, $-NR^{13}SO_2NR^{13}$-,-CO-, -OCO-, or -C(O)O- where n1 is 0-2, R^{12} hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl and each R^{13} is hydrogen or alkyl) wherein the aromatic or alicyclic ring in R^6 and R^{6a} is optionally substituted with one, two, or three R^a independently selected from alkyl, haloalkyl, alkoxy, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, amino, monsubstituted amino, disubstituted amino, nitro, aryloxy, benzyloxy, acyl, alkylsulfonyl, or arylsulfonyl where the aromatic or alicyclic ring

in R^a is optionally substituted with one or two substituents independently selected from alkyl, halo, alkoxy, haloalkyl, haloalkoxy, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl; or

R^5 and R^6 and R^{5a} and R^{6a} taken together with the carbon atom to which both R^5 and R^6 and R^{5a} and R^{6a} are attached form (i) cycloalkylene optionally substituted with one or two R^b independently selected from alkyl, halo, alkylamino, dialkylamino, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroaralkyl, alkoxycarbonyl, or aryloxycarbonyl or (ii) heterocycloalkylene optionally substituted with one to four alkyl or one or two R^c independently selected from alkyl, haloalkyl, hydroxy, hydroxyalkyl, alkoxyalkyl, alkoxyalkyloxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, aminoalkyl, acyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl, cycloalkyl, cycloalkylalkyl, $-S(O)_{n2}R^{14}$, -alkylene-$S(O)_{n2}$-R^{15}, $-COOR^{16}$, -alkylene-$COOR^{17}$, $-CONR^{18}R^{19}$, or -alkylene-$CONR^{20}R^{21}$ (where n2 is 0-2 and R^{14}-R^{17}, R^{18} and R^{20} are independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, or heterocycloalkyl and R^{19} and R^{21} are independently hydrogen or alkyl) wherein the aromatic or alicyclic ring in the groups attached to cycloalkylene or heterocycloalkylene is optionally substituted with one, two, or three substituents independently selected from alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, benzyl, alkoxy, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, amino, monsubstituted amino, disubstituted amino, or acyl;

R^7 is hydrogen or alkyl;

R^8 is hydroxy; or

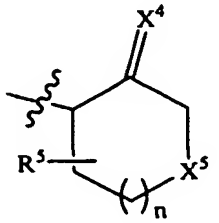
R^7 and R^8 together form oxo;

R^9 is hydrogen, halo, alkyl, aralkyl or heteroaralkyl;

R^{10} is alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, or heterocycloalkylalkyl wherein the aromatic or alicyclic ring in R^{10} is optionally substituted with one, two, or three R^d independently selected from alkyl, haloalkyl, alkoxy, alkoxyalkyl, cycloalkyl, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, aminosulfonyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, aryl, aralkyl, heteroaryl, amino, monsubstituted amino, disubstituted amino, carbamoyl, or acyl wherein the aromatic or alicyclic ring in R^d is optionally substituted with one, two, or three substitutents independently selected from alkyl, haloalkyl, alkoxy, haloalkoxy, halo, hydroxy, carboxy, alkoxycarbonyl, amino, alkylamino, or dialkylamino; and

R^{11} is hydrogen or alkyl; or

(iii) a group of formula (a):



(a)

where:

n is 0, 1, or 2;

X^4 is selected from $-NR^{22}$-, -S-, or –O- where R^{22} is hydrogen, alkyl, or alkoxy; and

X^5 is –O-, -S-, $-SO_2$-, or $-NR^{23}$- where R^{23} is selected from hydrogen, alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, aminoalkyl, acyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, $-S(O)_2R^{24}$, -alkylene-$S(O)_{n3}$-R^{25}, $-COOR^{26}$, -alkylene-$COOR^{27}$, $-CONR^{28}R^{29}$, or -alkylene-$CONR^{30}R^{31}$ (where n3 is 0-2 and R^{24}-R^{27}, R^{28} and R^{30} are independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, or heterocycloalkylalkyl and R^{29} and R^{31} are independently hydrogen or alkyl) where the aromatic or alicyclic ring in X^5 is optionally substituted with one, two, or three substituents independently selected from alkyl, haloalkyl, alkoxy, haloalkoxy, halo, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl and one substitutent selected from aryl, aralkyl, heteroaryl, or heteroaralkyl;

R^5 is as defined above;

R^1 is hydrogen or alkyl;

R^{1a} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkylalkyl, or –alkylene-X^2-R^{32} [wherein X^2 is $-NR^{33}$-, -O-, -$S(O)_{n4}$-, -CO-, -COO-, -OCO-, $-NR^{33}CO$-, $-CONR^{33}$-, $-NR^{33}SO_2$-, $-SO_2NR^{33}$-, $-NR^{33}COO$-, $-OCONR^{33}$-, $-NR^{33}CONR^{34}$, or $-NR^{33}SO_2NR^{34}$- (where R^{33} and R^{34} are independently hydrogen, alkyl, or acyl and n4 is 0-2) and R^{32} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, or heterocycloalkylalkyl] wherein said alkylene chain is optionally substituted with one to six halo and wherein the aromatic or alicyclic ring in R^{1a} is optionally substituted with one, two, or three R^e independently selected from alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, arylsulfonyl, aminocarbonyl, aminosulfonyl, acyl, hydroxy, haloalkoxy, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryloxycarbonyl, aryl, heteroaryl, cycloalkyl, cycloalkylalkyl, aralkyl, heteroaralkyl, amino, monsubstituted amino, disubstituted amino, or acyl; or

R^1 and R^{1a} together with the carbon atoms to which they are attached form cycloalkylene

or heterocycloalkylene ring wherein said cycloalkylene or heterocycloalkylene is optionally substituted with one or two R^f independently selected from alkyl, halo, haloalkyl, hydroxyalkyl, keto, or $-SO_2R$ where R is alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl or heteroaralkyl where the aromatic or alicylic ring in R^f is optionally substituted with one, two, or three substitutents independently selected from alkyl, alkoxy, haloalkyl, haloalkoxy, hydroxy, halo, carboxy, or alkoxycarbonyl;

R^2 is hydrogen or alkyl;

R^3 is hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl, amino, mono or disubstituted amino, or –alkylene-X^3-R^{35} [wherein X^3 is $–NR^{36}$-, -O-, $-S(O)_{n5}$-, -CO-, -COO-, -OCO-, $-NR^{36}CO$-, $-CONR^{36}$-, $-NR^{36}SO_2$-, $-SO_2NR^{36}$-, $-NR^{36}COO$-, $-OCONR^{36}$-, $-NR^{36}CONR^{37}$-, or $–NR^{36}SO_2NR^{37}$- (where R^{36} and R^{37} are independently hydrogen, alkyl, or acyl and n5 is 0-2) and R^{35} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl] wherein the aromatic or alicyclic rings in R^3 are optionally substituted by one, two, or three R^g independently selected from alkyl, halo, hydroxy, alkoxy, haloalkyl, haloalkoxy, oxo, cyano, nitro, acyl, acyloxy, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, aryloxy, benzyloxy, carboxy, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, arylthio, arylsulfonyl, arylsulfinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, amino, monosubsituted or disubstituted amino, and further wherein the aromatic and alicyclic rings in R^g are optionally substituted with one, two, or three R^h wherein R^h is independently selected from alkyl, halo, haloalkyl, haloalkoxy, hydroxy, nitro, cyano, hydroxyalkyl, alkoxy, alkoxyalkyl, aminoalkyl, alkylthio, alkylsulfonyl, amino, alkylamino, dialkylamino, aryl, heteroaryl, cycloalkyl, carboxy, carboxamido, or alkoxycarbonyl;

R^4 is hydrogen, alkyl, hydroxy, nitrile, or $–(alkylene)n_6$-X^6-R^{38} (where X^6 is –O-, $-NR^{39}$-, $-S(O)_{n7}$-, $–NR^{39}CO$-, -CO-, or -OC(O)- where n6 is 0 or 1, n7 is 0-2, and R^{39} is hydrogen or alkyl) and R^{38} is hydrogen, alkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, benzoxazolyl, or quinoxalinyl where R^{38} is optionally substituted with one, two, or three R^i independently selected from alkyl, alkoxy, halo, haloalkyl, haloalkoxy, hydroxy, alkylthio, alkylsulfonyl, arylsulfonyl, aminosulfonyl, acyl, amino, monosubstituted amino, disubstituted amino, carboxy, alkoxycarbonyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aryl, heteroaryl, or

heterocycloalkyl where the aromatic or alicyclic ring in R^i is optionally substituted with one or two substituents independently selected from alkyl, halo, alkoxy, haloalkyl, haloalkoxy, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl; or

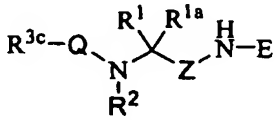
R^3 and R^4 in (Ia) or (Ib) together with the atoms to which they are attached form heteroaryl or heterocycloalkyl ring optionally fused to an aryl or heteroaryl ring wherein said rings are optionally substituted on the aromatic and/or non-aromatic portion of the rings with one, two, or three R^j;

each R^j and R^{4a} is independently:

hydrogen, alkyl optionally interrupted by one or two N, O, C(O), S, S(O), or $S(O)_2$ and optionally substituted by amino, hydroxy, halo, alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, benzoxazolyl or quinoxalinyl;

halo, alkoxy, alkylthio, hydroxy, carboxy, aryl, aryloxy, aroyl, heteroaryl, alkanoyl, -C(O)OR where (R is hydrogen, alkyl, alkoxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, aryl, arylalkyl, aminoalkyl, heterocycloalkyl, or heterocycloalkylalkyl), aminocarbonyl, aminosulfonyl, alkylsulfonyl, aryloxycarbonyl, benzyloxycarbonyl, alkanoylamino, alkylaminocarbonyl, dialkylaminocarbonyl, alkoxycarbonylamino, aroylamino, amino, alkylamino, dialkylamino, alkylthio, arylthio, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, cycloalkyl, benzyloxy, or ureido wherein each of the aforementioned groups in R^{4a} and R^j is optionally substituted with one, two, or three substituents independently selected from halo, hydroxy, alkyl, alkoxy, haloalkyl, haloalkoxy, oxo, carboxy, nitrile, nitro or $NH_2C(O)$-; or

(b) a compound of Formula (II):



(II)

where:

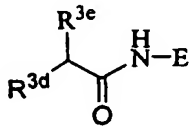
E, R^1, R^{1a} and R^2 are as defined above;

Z is –CO- or $–CH_2SO_2$-; or

Q is –CO-, $-SO_2$-, -OCO-, -NRCO-, or $–NRSO_2$- where R is hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, or aralkyl;

R^{3c} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl, or –alkylene-X^8-R^{40} [wherein X^8 is $–NR^{41}$-, -O-, $-S(O)_{n8}$-, -CO-, -COO-, -OCO-, $-NR^{41}CO$-, $-CONR^{41}$-, $-NR^{41}SO_2$-, $-SO_2NR^{41}$-, $-NR^{41}COO$-, $-OCONR^{41}$-, $-NR^{41}CONR^{42}$-, or $–NR^{41}SO_2NR^{42}$- (where each R^{41} and R^{42} is independently hydrogen, alkyl, or acyl and n8 is 0-2) and R^{40} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl] wherein the alkylene chain in R^{3c} is optionally substituted with one to three halo atoms and the aromatic and alicyclic rings in R^{3c} are optionally substituted by one, two, or three R^k independently selected from alkyl, aminoalkyl, halo, hydroxy, alkoxy, haloalkyl, haloalkoxy, oxo, cyano, nitro, acyl, acyloxy, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryloxy, benzyloxy, carboxy, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, arylthio, arylsulfonyl, arylsulfinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, aralkylaminosulfonyl, aminocarbonyl, arylaminocarbonyl, aralkylaminocarbonyl, amino, monosubsituted or disubstituted amino, and further wherein the aromatic and alicyclic rings in R^k are optionally substituted with one, two, or three R^l wherein R^l is independently selected from alkyl, halo, haloalkyl, haloalkoxy, hydroxy, nitro, cyano, hydroxyalkyl, alkoxy, alkoxyalkyl, aminoalkyl, alkylthio, alkylsulfonyl, amino, monosubstituted amino, dialkylamino, aryl, heteroaryl, cycloalkyl, carboxy, carboxamido, or alkoxycarbonyl; or

(c) a compound of Formula (III):



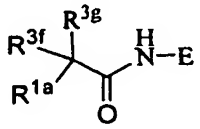
(III)

where E is as defined above;

R^{3d} and R^{3e} are independently –alkylene-X^9-R^{43} [wherein X^9 is bond, $–NR^{44}$-, -O-, $-S(O)_{n9}$-, -CO-, -COO-, -OCO-, $-NR^{44}CO$-, $-CONR^{44}$-, $-NR^{44}SO_2$-, $-SO_2NR^{44}$-, $-NR^{44}COO$-, $-OCONR^{44}$-, $-NR^{44}CONR^{45}$-, or $–NR^{44}SO_2NR^{45}$- (where R^{44} and R^{45} are independently hydrogen, alkyl, or acyl and n9 is 0-2) and R^{43} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, or heterocycloalkylalkyl] wherein the alkylene chain is optionally substituted with one to three halo atoms and the aromatic or alicyclic rings in R^{3d} and R^{3e} are optionally substituted by one, two, or three R^m independently selected from alkyl, halo,

hydroxy, alkoxy, haloalkyl, haloalkoxy, oxo, cyano, nitro, acyl, acyloxy, carboxy, alkoxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkylcarbamoyloxy, alkylsulfonylamino, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, aminocarbonyl, amino, monosubsituted or disubstituted amino and one R^m selected from aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryloxy, benzyloxy, aryloxycarbonyl, arylthio, arylsulfonyl, arylsulfinyl, aryloxycarbonylamino, arylcarbamoyloxy, arylsulfonylamino, arylaminosulfonyl, or aralkylaminosulfonyl wherein the aromatic or alicyclic ring in R^m is optionally substituted with one, two, or three R^n wherein R^n is independently selected from alkyl, halo, haloalkyl, haloalkoxy, hydroxy, nitro, cyano, hydroxyalkyl, alkoxy, alkoxyalkyl, aminoalkyl, alkylthio, alkylsulfonyl, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heteroaralkylsulfonylamino, amino, monosubstituted amino, dialkylamino, aryl, heteroaryl, cycloalkyl, carboxy, carboxamido, or alkoxycarbonyl; or

(d) a compound of Formula (IV):



(IV)

where:

E and R^{1a} are as defined above;

R^{3f} is hydrogen;

R^{3g} is hydrogen, fluoro, $-OR^{46}$ or $-NR^{47}R^{48}$ where:

R^{46} is hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl, –(alkylene)n_{10}-X^{10}-R^{49} [wherein n10 is 0 or 1, X^{10} is -CO- or $-CONR^{50}$- where R^{50} is hydrogen, alkyl, or alkoxyalkyl, and R^{49} is hydrogen, alkyl, haloalkyl, alkoxyalkyl, hydroxyalkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroaralkyl, heterocycloalkyl or heterocycloalkylalkyl or R^{49} and R^{50} together with the nitrogen atom to which they are attached from heterocycloalkyl], or –alkylene-X^{11}-R^{51} [wherein X^{11} is $–NR^{52}$-, -O-, $-S(O)_{n11}$-, -COO-, -OCO-, $-NR^{52}CO$-, $-NR^{52}SO_2$-, $-SO_2NR^{52}$-, $-NR^{52}COO$-, $-OCONR^{52}$-, $-NR^{52}CONR^{53}$-, or $–NR^{52}SO_2NR^{53}$- where n11 is hydrogen or alkyl, R^{52} is hydrogen or alkyl, and R^{51} is hydrogen, alkyl, haloalkyl, alkoxyalkyl, hydroxyalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl or heterocycloalkylalkyl or R^{51} together with R^{52} or R^{53} in $-SO_2NR^{52}$-, $-OCONR^{52}$-, $-NR^{52}CONR^{53}$-, or $–NR^{52}SO_2NR^{53}$- form heterocycloalkyl] wherein the alkylene chain is optionally substituted

with one to three halo atoms and the aromatic or alicyclic rings in R^{46} are optionally substituted by one, two, or three R^o independently selected from alkyl, halo, hydroxy, alkoxy, hydroxyalkyl, alkoxyalkyl, haloalkyl, haloalkoxy, oxo, cyano, nitro, acyl, acyloxy, carboxy, alkoxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkylcarbamoyloxy, alkylsulfonylamino, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, aminocarbonyl, amino, monosubsituted or disubstituted amino and one R^o selected from aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryloxy, benzyloxy, aryloxycarbonyl, arylthio, arylsulfonyl, arylsulfinyl, aryloxycarbonylamino, arylcarbamoyloxy, arylsulfonylamino, arylaminosulfonyl, or aralkylaminosulfonyl wherein the aromatic and alicyclic rings in R^o are optionally substituted with one, two, or three R^p wherein R^p is independently selected from alkyl, halo, haloalkyl, haloalkoxy, hydroxy, nitro, cyano, hydroxyalkyl, alkoxy, alkoxyalkyl, aminoalkyl, alkylthio, alkylsulfonyl, amino, monosubstituted amino, dialkylamino, aryl, heteroaryl, cycloalkyl, carboxy, carboxamido, or alkoxycarbonyl;

R^{47} is hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, or heterocycloalkylalkyl; and

R^{48} is hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, aryloxycarbonyl, aralkyloxycarbonyl, heteroaryloxycarbonyl, heteroaralkyloxycarbonyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, or heterocycloalkylalkyl provided that one of R^{47} and R^{48} is other than hydrogen and wherein the aromatic or alicyclic rings in R^{47} and R^{48} are optionally substituted by one, two, or three R^q independently selected from alkyl, halo, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, haloalkyl, haloalkoxy, oxo, cyano, nitro, acyl, acyloxy, carboxy, alkoxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkylcarbamoyloxy, alkylsulfonylamino, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, amino, monosubsituted or disubstituted amino and one R^q selected from aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryloxy, benzyloxy, aryloxycarbonyl, arylthio, arylsulfonyl, arylsulfinyl, aryloxycarbonylamino, arylcarbamoyloxy, arylsulfonylamino, arylaminosulfonyl, or aralkylaminosulfonyl wherein the aromatic and alicyclic rings in R^q are optionally substituted with one, two, or three R^r wherein R^r is independently selected from alkyl, halo, haloalkyl, haloalkoxy, hydroxy, nitro, cyano, hydroxyalkyl, alkoxy, alkoxyalkyl, aminoalkyl, alkylthio, alkylsulfonyl, amino, monosubstituted amino, dialkylamino, aryl, heteroaryl, cycloalkyl, carboxy, carboxamido, or alkoxycarbonyl; or

R^{3f} and R^{3g} are fluoro;

(l) 7-(2,2-dimethylpropyl)-6-thiophen-2-ylmethyl-7H-pyrrolo-[2,3-d]pyrimidine-2-carbonitrile;

(m) morpholine-4-carboxylic acid [(*S*)-1-(4-cyano-1-methylpiperidine-4-ylcarbamoyl)-4,4-dimethylhexyl]amide;

(n) morpholine-4-carboxylic acid [(*S*)-1-(4-cyano-1-propylpiperidine-4-ylcarbamoyl)-3,3,4,4-tetramethylpentyl]amide;

(o) morpholine-4-carboxylic acid [(*S*)-1-(4-cyano-1-propylpiperidine-4-ylcarbamoyl)-4,4-dimethylpentyl]amide;

(p) morpholine-4-carboxylic acid [(*S*)-1-(4-cyano-1-propylpiperidine-4-ylcarbamoyl)-4,4-dimethylhexyl]amide;

(q) morpholine-4-carboxylic acid [(*R*)-1-(4-cyano-1-methylpiperidine-4-ylcarbamoyl)-4,4-dimethylhexyl]amide;

(r) 5,5-dimethyl-2-(2-oxo-2H-benzo[e][1,3]oxazin-4-ylamino)heptanoic acid (4-cyano-1-propylpiperidin-4-yl)amide;

(l) 5,5-dimethyl-2-(2-oxo-2H-benzo[e][1,3]oxazin-4-ylamino)heptanoic acid (4-cyano-1-(3-morpholin-4-ylpropyl)piperidin-4-yl)amide;

(m) 5,5-dimethyl-2-(2-oxo-2H-benzo[e][1,3]oxazin-4-ylamino)heptanoic acid (4-cyano-1-(2-morpholin-4-ylethyl)piperidin-4-yl)amide;

(n) 5,5-dimethyl-2-(2-oxo-2H-benzo[e][1,3]oxazin-4-ylamino)heptanoic acid {4-cyano-1-[2-(2-methoxyethoxy)ethyl]piperidin-4-yl}amide;

(o) 5,5-dimethyl-2-(2-oxo-2H-benzo[e][1,3]oxazin-4-ylamino)heptanoic acid (4-cyano-1-methylpiperidin-4-yl)amide;

(p) 2-(7-fluoro-2-oxo-2H-benzo[e][1,3]oxazin-4-ylamino)-5,5-dimethylheptanoic acid (4-cyano-1-propylpiperidin-4-yl)amide;

(q) 2-(7-fluoro-2-oxo-2H-benzo[e][1,3]oxazin-4-ylamino)-5,5-dimethylhexanoic acid {4-cyano-1-(2-morpholin-4-ylethyl)piperidin-4-yl}amide; or

(r) 2-(7-fluoro-2-oxo-2H-benzo[e][1,3]oxazin-4-ylamino)-5,5-dimethylhexanoic acid {4-cyano-1-[2-(2-methoxyethoxy)ethyl]piperidin-4-yl}amide; or

a pharmaceutically acceptable salt thereof.

21. Use of a Cathepsin S inhibitor for the manufacture of a medicament for combination therapy with a biologic.

22. Use of a Cathepsin S inhibitor for the manufacture of a medicament for combination therapy with a biologic wherein the Cathepsin S inhibitor treats the immune response caused by the biologic.

23. The use of Claim 21 or 22 wherein the biologic is a protein.

24. The use of Claim 21 or 22 wherein the biologic is an antibody.

25. The use of Claim 21 or 22 wherein the biologic is Remicade®, Refacto®, Referon-A®, Factor VIII, Factor VII, Betaseron®, Epogen®, Embrel®, Interferon beta, Botox®, Fabrazyme®, Elspar®, Cerezyme®, Myobloc®, Aldurazyme®, Verluma®, Interferon alpha, Humira®, Aranesp®, Zevalin® or OKT3.